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BACTERIOLOGICAL DIAGNOSIS OF DIPHTHERIA.

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The critical student of medicine in his daily study of disease, has continually before him two objective points, namely, the successful treatment of his case, and the clear conception to himself of just what pathological conditions obtain. You may say that these two attainments are interdependent—they ought always to be, but too frequently are independent of each other. It is unfortunately a necessity of our imperfect medical knowledge that the diagnosis has to be often held in abeyance, while the progress of the case and the sentiments of the family both serve to render an accurate diagnosis of small moment to the physician. The diagnosis of a case is *a priori* the first step in its treatment, but the practising physician knows from experience that the most studied diagnosis does not appeal to the patient in any degree as do speedy active measures for his relief. But when the diagnosis itself is of the most vital importance not only to the physician but to the patient, his family, and the entire community as well, the physician is bound to use all the means scientific medicine has given him to meet the emergency squarely and promptly.

Prominent among the cases of the general practitioner is the very large class of "sore throats," many of which are frequently dismissed with a prescription, and the remark "it 's nothing but a sore throat." Happily for the other members of society, this easy assumption of a benign affection is becoming less and less common, and the unconscious spreading of diphtheria is becoming more and more restricted. The germ theory of disease stands to-day on no uncertain ground, as the established bacteriolog-

ical etiology of typhoid-fever, cholera, tetanus, erysipelas, relapsing fever and many others, abundantly testifies. It is the hope of the upholders of this theory to demonstrate a similar etiology in all acute diseases, and this expectation is steadily becoming a reality.

The foundation on which the bacteriological diagnosis of diphtheria rests, consists in the now thoroughly attested fact, that this disease is due to a specific micro-organism which can be readily isolated and demonstrated, by culture from swabbings of the mucous membranes affected. The early bacteriologists attempted to locate the infecting agent of diphtheria in the blood, but numerous examinations failed to demonstrate the presence of micro-organisms in it. Later a variety of bacteria were found in the pseudo membrane in diphtheria, and as more extended researches have proven, the specific bacterium of this disease was first recognized by Klebs in 1883, and cultivated and described in 1884 by Loeffler and is called the Klebs-Loeffler bacillus. This organism is rod-shaped, two or three thousandths of an inch in length, and has a characteristic morphology. It appears generally as a rod swollen at either end or in the middle or made up of irregular segments. It grows freely in the presence of oxygen at the body temperature, and in dried fragments of diphtheritic membrane preserves its vitality for months. It may be found not only in the exudate of pharynx, larynx, or nose, but also in almost any local morbid condition which may be concurrent. I have personally observed it in a purulent discharge from the middle ear, in the secretion of an ulcerated area after vaccination, in pus from an abscess of the leg and a paronychia of the toe, all of these lesions being coincident with the diphtheria for which these cases were brought to the Boston City Hospital.

The technique of its identification is as follows: Sterilized cotton swabs are wiped across the mucous membrane affected, and are then wiped over the surface of the sterilized culture media. It is possible to find the bacilli by direct examination of the secretion, by rubbing the swab on a clean cover glass, staining in the usual way, and microscopic examination; but the bacilli are relatively so few in number in such a stained preparation that a negative result is not sufficient evidence of

their absence in the case in question. Various culture media may be used for the cultivation of the bacilli—sterilized potato, nutrient agar or gelatine, and simple blood serum. Loeffler has suggested a mixture of blood serum and sugar bouillon, and this is now commonly used in making cultures of Klebs-Loeffler bacilli. It is easy to make, gives a very characteristic growth, and is found to present the most favorable conditions for their cultivation. The medium consists of three parts beef blood serum, and one part of a one per cent. sugar bouillon, solidified in slanting test tubes at a low temperature, and sterilized by steam. Having inoculated a test tube of the serum with the swab, the tube is then placed in an incubator, kept at a temperature of 37° Centigrade for twenty-four hours. At the end of this time numerous aggregations or colonies of Klebs-Loeffler bacilli appear on the surface of the serum, as small, raised, rounded, dry-looking elevations. With a sterilized platinum needle a cover glass is smeared with a single colony, stained with one of the aniline dyes—methaline blue in an alkaline solution being the best—and the cover glass then mounted in balsam and examined under a microscope, using an oil immersion lens of at least one twelfth inch power.

The evidence to-day is stronger than ever that the bacterium in question is the specific infecting agent of diphtheria, and I cannot do better than give a resumé of the principal points made by Loeffler in his demonstration in 1890.

First. "It is found in all undoubted cases of diphtheria." The careful and extended researches of bacteriologists of many countries support this statement, such as Loeffler, Von Hoffmann, Ortman, Roux and Yersen, Biggs, Welch and Abbott, and Prudden. The number of cases which seemingly refute this statement is steadily decreasing, as experience in examination and improved methods of technique constantly develop. In doubtful cases a single examination is never sufficient, and in apparently definite clinical cases, repeated examinations must be made before a negative result can be claimed.

Second. "The Klebs-Loeffler bacillus is found only in diphtheria." Numerous cases were formerly reported in which this bacillus was found in the throats of healthy children but these cases are open to grave doubt, and it is to be noted that such

cases are rarely heard of to-day. The recognition of very mild cases of diphtheria is now not only possible but imperative, as it is abundantly proven that cases of severer types may emanate from these mild in form.

Third. "As shown by Loeffler's earliest researches pure cultures of this bacillus induce characteristic diphtheritic inflammation when inoculated into the mucous membrane of certain lower animals," notably rabbits and guinea pigs. This statement is being daily demonstrated in our laboratories and needs no comment.

It was not long after the discovery of the specific infecting agent of diphtheria that it became a matter of almost daily occurrence to find this bacillus in throats whose clinical appearance was not that of diphtheria, and further its absence was noted in cases that presented the typical diphtheritic pseudo-membrane. The former class showed us beyond a doubt that mild cases of diphtheria are common, and probably have not been recognized as such in the past; while the latter cases raised a reasonable doubt in our minds as to the dependence to be placed in this new method of diagnosis. But continued study of the micro-organisms found in these various affections of the throat has given us the following resumé of the etiology of diphtheritic and pseudo-diphtheritic inflammations: the mouths of most people always contain a variety of micro-organisms, two of the most common being the streptococcus, and the staphylococcus Pyogenes Aureus. Under favorable conditions either one or both of these germs become greatly increased in number, and infecting the mucous membrane at some point, produce the condition of inflammation, varying in degree from one of simple congestion to that of the clinical appearance of diphtheria. Pure cultures of streptococci are commonly found in this latter class of non-diphtheritic cases, and they are usually milder and not as contagious as cases due to the Klebs-Loeffler bacillus. Occasionally, however, the septic condition is very severe, and is often so when complicated by scarlet fever or measles.[1] These cases should always be isolated, and treated as mildly infectious affections. Mixed infections of some of the

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[1] Manual of Bacteriology. Sternberg.

pyogenic bacteria with the Klebs-Loeffler bacilli are not uncommon, and are not to be lightly regarded.

Infection by the Klebs-Loeffler bacilli may produce almost no signs or symptoms, these cases being of very short duration, the non-susceptibility of the patient accounting for the lack of disturbance. Such cases are to be regarded as sources of danger, and persons in charge of diphtheria cases whose throats may temporarily show these bacilli are also to be so regarded.[1] Daily bacteriological examinations are to be made in all doubtful cases until the diagnosis is clear. It may be mentioned here that patients convalescent from diphtheria are to be regarded as sources of danger as long as Klebs-Loeffler bacilli are found to be present by bacteriological examination ; and they have been found in such cases from a few days to three months after the disappearance of all membrane.

The cases which have been brought up to disprove the reliability of the Klebs-Loffler bacillus as the sole infecting agent in diphtheria may be explained in part by the fact that we frequently meet with a bacillus resembling the Klebs-Loeffler, but constantly differing from it, apparently having no connection with diphtheria and being non-virulent.

In this very brief presentation of so important a subject as the diagnosis of diphtheria, I wish to emphasize very forcibly the advantage not for the purposes of treatment or prognosis, but for diagnosis alone, of the early bacteriological examination of all suspicious cases. The very careful and painstaking attention which the boards of health of the large cities are officially giving this very matter, bears testimony to the great importance in which it is held by the leaders in medical thought in the country.

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[1] *New York Medical Record*, March 25, 1895.